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ATARAX AND VISTARIL

Hydroxyzine hydrochloride (Atarax-Roerig Div. of Pfizer) and hydroxyzine pamoate (Vistaril-Pfizer) are essentially the same drug, and both are offered in tablet and liquid form for the treatment of a wide range of emotional disorders, including hyperkinetic and tension states in children. Hydroxyzine is also promoted for the management of cardiac arrhythmias and allergic disorders. The drug is a disubstituted derivative of piperazine having the same general chemical configuration as such antihistaminic drugs as chlorcyclizine (Di-Paralene-Abbott) and meclizine (Bonamine-Pfizer).

Hydroxyzine has been shown to have antihistaminic, antiemetic and hypothermic effects (S. Levis, et al., Arch. int'l Pharmacodyn., 109:127, 1957). Some of these effects are also shown by chlorpromazine (Thorazine), but hydroxyzine in reasonable doses does not modify the general demeanor of experimental animals as does chlorpromazine, and the psychological effects of the two drugs in humans do not appear to be similar in any substantial way. In fact, no specific behavioral effects of hydroxyzine in experimental animals or human patients have been conclusively established by pharmacologic studies. Clinically, the hydroxyzine drugs are reported to relieve mild tension and anxiety without impairing critical faculties.

EFFECTS IN CHILDREN - The enthusiastic clinical reports on these drugs in emotional disturbances in adults are based largely on uncontrolled observations. In one controlled study of hydroxyzine in subnormal, maladjusted children (L. J. Segal and A. E. Tansley, J. Mental Sci., 103:677, 1957), improvement in work and behavior was reported. This effect has not been confirmed by Medical Letter consultants having extensive experience with disturbed children. The drug is claimed to have special usefulness in relieving hyperkinetic states in children, but convincing evidence to support this claim is lacking.

Successful use of hydroxyzine in the treatment of cardiac arrhythmias has been reported. The claim that the drug has a direct action on the myocardium may have some foundation, but the implication that such action plays a role in the clinical control of cardiac arrhythmias is not yet justified by the evidence available. In one study (W. Wright, JAMA, 171:1642, 1959) hydroxyzine was reported to be helpful in the management of nummular eczema, but the study was uncontrolled; no beneficial effects were noted in other dermatoses.

Hydroxyzine is usually well tolerated. While such side effects as increased intestinal peristalsis, dry mouth, unsteadiness and muscular weakness have been reported, they have been infrequent. The most that can be said for hydroxyzine at present is that it has the usefulness and limitations of a sedative. In agitated psychotic patients, it will not provide the therapeutic effects obtained with reserpine or with chlorpromazine.

CALURIN

Aspirin, one of the most useful and certainly the most used of all drugs, has its share of disadvantages, and many efforts have been made to overcome them. For a time, the claim that the addition of buffering agents, as in Bufferin, increased the speed of absorption of aspirin and diminished its tendency to cause gastric irritation, was widely accepted; but many studies have shown that in both these respects buffered aspirin is indistinguishable from plain aspirin (The Medical Letter, 1:7, 1959).

Now, physicians are being urged to prescribe more soluble salicylates or "aspirins" in place of plain aspirin. One of these, Calurin (Smith-Dorsey), is calcium acetyl salicylate carbamide, the most soluble acetyl ester of salicylic acid. Calurin is more rapidly absorbed than aspirin, but there is no evidence that it offers a clinically significant advantage in the rate at which analgesic effects are achieved. It is of interest that there is poor correlation between salicylate blood levels and the intensity and duration of analgesic effect.

GASTRIC EFFECTS - The chief advantage claimed for the greater solubility of Calurin is the absence of damaging effects on the gastric mucosa. So far as systemic effects are concerned, calcium acetyl salicylate has all of the pharmacologic and toxic properties of other salicylates. According to Goodman and Gilman (The Pharmacological Basis of Therapeutics, 2nd Edition, Macmillan, 1958, p. 295) and other authors, most of the gastrointestinal side effects occurring after intensive salicylate therapy, as for rheumatic disorders, are attributable to the central-nervous-system action of the drug, and are directly related to blood-salicylate levels. Contrary to the general impression, aspirin - a very weak acid - does not increase stomach acidity (R. Rubin, et al., N. E. J. Med., 261:1208, Dec. 10, 1959). The usefulness of bicarbonate of soda and similar alkaline salts in lessening the gastric irritation which aspirin causes in some persons results not from antacid action, but primarily from their effectiveness in promoting more rapid gastric emptying (H. Shay and J. Gershon-Cohen, Surg. Gyn. and Obs., 58:935, 1944).

The main question is whether the primary irritating or erosive effect of aspirin on the stomach mucosa is such that the use of a more soluble product is indicated; on this point there have been controversy and conflicting findings. A review by A. Muir and I. A. Cossar (Lancet, 1:539, 1959) indicates that in some persons ordinary doses of aspirin can cause an acute erosive gastritis (with indigestion and bleeding) when large particles of aspirin are trapped and adhere in the rugae. But this risk is minimized when aspirin is taken with meals rather than on an empty stomach, or when it is taken with a full glass of water (the pa-

tient should be carefully instructed on this point). While aspirin sometimes causes acute erosive gastritis in the absence of trapped particles, it has not been established that this effect is less frequent after soluble aspirin than after plain aspirin.

To summarize, Calurin has not been shown to have any significant therapeutic advantage over aspirin; in terms of gastrointestinal effects, however, particularly gastric bleeding, it may be preferable for some patients on large and prolonged dosage, though the difference is probably minimized or eliminated if aspirin is taken with meals or with a full glass of water. Where cost is of no concern, Calurin may well be used instead of aspirin; but for the great majority of patients the extra expense is not warranted. Each tablet of Calurin contains the equivalent of 5 gr. of aspirin and costs about 5¢. The most expensive brands of plain aspirin, USP, cost less than a cent a tablet.

APPETITE DEPRESSANTS

The chain of events leading to clinical obesity is, in most instances, dominated by emotional and familial factors that stimulate or exaggerate appetite, and sustained weight reduction in the truly obese is not easy to achieve or to maintain. A medically supervised weight-control program should include painstaking and persistent dietary instruction, cautions where needed about drinking (alcoholic) habits, and psychotherapy. Encouragement of moderate exercise or sports activities is also desirable (J. Mayer, Postgrad. Med., 25: 325, 1959). In some persons, obesity is a somatic adaptation to intense emotional conflict and is reversed at peril to the adaptation (A. J. Stunkard, Am. J. Med., 23: 77, 1957). In those instances of obesity where dieting, psychotherapy and exercise have had an adequate trial and have not been successful, the addition of an appetite-depressing drug may give gratifying results. In most cases, however, the effects will be only temporary.

Over 30 ethical drugs are available for appetite depression. Almost all are sympathomimetic drugs which are either isomers, congeners, variants, or distant relatives of the mother appetite-depressant drug, amphetamine sulfate. The chief advantage claimed for most of the newer amines over dextro-amphetamine is effective appetite depression without central-nervous-system stimulating action or side effects. Whether this advantage has actually been achieved with any effective preparation is open to question. Appraisals of the newer preparations will be carried in later issues.

DEXTRO-AMPHETAMINE - The standard and probably the most widely used appetite-depressing drug is dextro-amphetamine sulfate, a USP preparation sold under the generic name by many companies and as Dexedrine by Smith, Kline & French. Its effectiveness in helping to depress appetite and thus reduce food intake has been established by well-controlled studies, particularly the classical report of S. C. Harris, et al. (JAMA, 134: 1469, 1947). Other studies have shown, however, that the appetite-reducing effect of the drug tends to diminish as tolerance is acquired, and often becomes insignificant after a few weeks or months.

Although the central-nervous-system stimulation produced by the amphetamines is undesirable in some patients, it may help other patients adhere to a diet by reducing the physical lethargy and mental depression that often accompany dieting or that are associated with overweight. The adrenergic vascular effects of the amphetamines, such as peripheral vasoconstriction and increase in heart rate, are usually no barrier to their effective use in appetite depression. These effects are, however, sufficiently important for the amphetamines to be used with caution in patients with coronary artery disease or severe hypertension. The more important central-nervous-system effects include increased wakefulness, alertness, and auditory and visual acuity.

DOSAGE - The dosage and the spacing of doses of dextro-amphetamine should be determined by individual needs and reactions to the drug. Many patients will respond to 2.5 mg. once or twice daily. Others may need as much as 15 or 20 mg. daily. If the drug causes insomnia, the last dose should not be taken later than mid-afternoon. On the other hand, a late afternoon dose may be most important for those who go on a food binge at night. Prolonged-release preparations of amphetamines should generally be avoided. Even when they are well formulated, the variable response of the digestive tract, even in the same person, makes the duration and intensity of action of such products unpredictable. Addiction to the amphetamines has been reported. Doses in the toxic range produce cardiac arrhythmias and toxic psychosis.

It seems clear that the amphetamines do not offer a royal road to weight reduction. But they are occasionally useful supplements to diet, moderate exercise and psychotherapy. Their effects are likely to be temporary, however. Dextro-amphetamine sulfate under its generic name costs about $2.50 to $3 per hundred 5-mg. tablets; as Dexedrine the cost is usually about $5 or $6.

TOPICAL CORTICOSTEROIDS - A CORRECTION

In a discussion of topical corticosteroids (The Medical Letter, 1:94, Dec. 11, 1959), it was stated that expert opinion differed on the relative merits of the various topical steroids; that some investigators considered triamcinolone acetonide (Kenalog-Squibb; Aristocort Topical-Lederle) to be more effective than the others, but that there were no controlled studies to support this view. Several controlled studies comparing 0.1% triamcinolone acetonide with 1% hydrocortisone have, in fact, been published. In one such study, J. G. Smith, Jr., et al. (AMA Arch. Derm., 78:643, 1958) found the triamcinolone acetonide more effective than the hydrocortisone in 75 of 109 patients with a variety of dermatoses. In a new controlled study comparing 0.1% triamcinolone acetonide with 1% hydrocortisone, 0.5% prednisolone, and 0.025% fluorometholone (M. M. Cahn and E. J. Levy, Antib. Med. & Clin. Ther., 6:734, Dec. 1959), the triamcinolone was found to be "significantly superior" to all of the other preparations. While further experience and controlled trials pairing all of the topical steroids in different concentrations are needed for an adequate understanding of the relative merits of the various preparations, there appears to be sound support for the views of those who believe that 0.1% triamcinolone acetonide shows superior effectiveness in many patients.

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